CDS-215 INVENTOR: Randy K. Bower, *et al.*
FAILURE DETECTION IN AUTOMATED CLINICAL ANALYZERS

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 506 022 A2**

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number: **92105149.6**

(22) Date of filing: **25.03.92**

(51) Int. Cl.5: **G01N 35/06, G01N 1/28**

(30) Priority: **26.03.91 JP 61669/91**

(43) Date of publication of application: **30.09.92 Bulletin 92/40**

(84) Designated Contracting States: **DE**

(71) Applicant: **Kabushiki Kaisha Toshiba**
72, Horikawa-cho Saiwai-ku
Kawasaki-shi(JP)

(72) Inventor: **Shinohara, Hiroo**
70-32, Higashimishima 4-Chome,
Nishinasuno-Machi
Nasu-Gun, Tochigi-ken(JP)

(74) Representative: **Blumbach Weser Bergen**
Kramer Zwirner Hoffmann Patentanwälte
Radeckestrasse 43
W-8000 München 60(DE)

(54) **Automatic chemical analysis system and automatic chemical analysis method.**

(57) An automatic chemical analysis sytem comprises a sample setting unit for accommodating a plurality of sample vessels each in which a sample is contained, a suction unit for sucking the sample in the sample vessel and detcting an amount of the sucked sample, a sample temporary storage unit for storing the sample vessel in which an insufficient amount of the sample is contained, a dilution unit for diluting the sample contained in the sample vessel stored in the sample temporary storage unit, a reagent setting unit for supplying a reagent into the sample vessel, a measurement unit including a sample reaction vessel into which the reagent is supplied from the reagent setting unit, and a control unit for controlling operations of these units. The control unit performs operations for instructing that a sample vessel containing the sufficient amount of the sample is to be directly transferred to the measurement unit and a sample vessel containing the insufficient amount of the sample is to be transferred to the sample temporary storage unit, for calculating an insufficient amount of the sucked sample in the sample vessel transferred to the sample temporary storage unit and for obtaining an information regarding an amount of a dilution solution for compensating for the insufficient amount of the sample, for carrying out an analysis treatment after dilution of the sample in accordance with the information of the amount of the dilution solution, and for compensating for a result of the analysis treatment in accordance with the information of the amount of the dilution solution.

EP 0 506 022 A2

sample temporary storage unit and associated units of the automatic chemical analysis system of Fig. 1;

Fig. 5 is an illustration for the explanatory of a dilution unit of the automatic chemical analysis system of Fig. 1; and

Fig. 6 is a flowchart for the explanatory of automatic chemical analyzing processes carried out according to the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

An automatic chemical analysis system to which the present invention is applicable generally comprises an analyzing unit and a data processing unit. The analyzing unit includes a sampler, i.e. sample setting unit, generally having a circular configuration and being rotatable, in which a plurality of sample vessels containing samples to be analyzed are set, a sample dilution means for diluting the sample as occasion demands and a measuring unit including a constant temperature container and an agitation means, for example for maintaining constant the temperature of the sample. In such the analysis system, these members are arranged on a table, for example, of the analyzing unit. A reagent supply container in which a reagent is contained is disposed in the vicinity of the sample analyzing unit.

The data processing unit includes an overall control unit as a central processing unit (CPU) provided with a display means or a printer. The data from or to the respective means are controlled by this data processing unit.

A preferred embodiment of the present invention will be described hereunder with reference to Figs. 1 to 6.

Fig. 1 is a diagram showing an arrangement of one embodiment of an automatic chemical analysis system according to the present invention, wherein a sample setting unit 1 includes a plurality of sample vessels 1A such as test tubes each containing a sample to be analyzed, these sample vessels 1A being sequentially moved. Fig. 1 shows the case in which only one sample vessel 1A is provided. Referring to Fig. 1, a sample suction probe 2 is disposed above the sample vessel 1A and can be vertically and horizontally moved by a drive unit 5. A pump 4 is connected to the sample suction probe 2 through a suction monitor 3 and the probe 2 sucks an amount of a sample necessary for analysis when it is lowered into the sample vessel 1A.

The suction monitor 3 has a function for detecting whether or not a necessary amount of the sample is sucked when the sample is sucked. A result of detection is supplied to an overall control unit 15 to be described hereinlater and it is determined on the basis of this result whether the sample is to be directly transferred to a direct measurement line 12 such as a route R3 or to be transferred to a temporary sample storage unit 6 such as a route R1.

A sample the amount of which sucked by the sample suction probe 2 is sufficient for analysis is directly tansferred to the measurement line 12 in a horizontal direction by being driven by the drive unit 5 and supplied to a reaction vessel 12A prepared in the measurement line 12, whereas the sample the sucked amount of which is not sufficient for analysis is transferred to the temporary sample storage unit 6 instead of being transferred to the measurement line 12.

A reagent setting unit 17 is disposed in the vicinity of the measurement line 12 from which a desired reagent is supplied to the reaction vessel 12A by a reagent gathering unit, not shown, almost at the same time with the supply of the sample. Further, when an indication of the dilution is made, pure water is supplied to the reaction vessel 12A from a dilution unit 13 through a dilution probe 13A. The result of anylysis of the sample subjected to an analyzing process at the measurement line 12 under the control of a measurement control unit 14 is supplied to the overall control unit 15 and reported to a display unit 16 composed of a CRT (cathod ray tube) monitor or printer.

The temporary sample storage unit 6 is composed of a sample vessel 6A such as test tube to which the sample transferred by the sample suction probe 2 is supplied, a sample quantity determination probe 7 which is to be lowered into the vessel 6A by a drive unit 9 for determining the quantity of the sample, a level detection unit 10 for detecting the level of the sample in the vessel 6A, a pump 8 for sucking the sample, a cleaning unit 11 for cleaning the vessel 6A, and the like. The shape and size of the sample vessel 6A to which an insufficient amount of a sample is supplied is previously known. The sample suction probe 2 having transferred a sample to the sample temporary storage unit 6 returns to the original position thereof at once for sucking other sample. Therefore, the operation of the sample suction probe 2 is carried out concurrently with the opeartion of the sample quantity determination prove 7.

The sample quantity determination probe 7 is lowered into the vessel 6A by the drive unit 9, and when the level detection unit 10 attached to the extreme end of the probe 7 detects the sample level, a detection signal is transmitted to the drive unit 9. With this arrangement, the drive unit 9 calculates an amount (volume) of the sample in the vessel 6A by calculating a moving amount of the probe 7 lowered into the vessel 6A and determin-

ing a height of the level of the sample based on the previously known shape and size of the vessel 6A.

Fig. 2 describes a method of calculating an amount of the sample as explained above. In Fig. 2, H0, H1, H2, V1 and S are defined as follows.

- H0: height from the bottom of the vessel 6A to the initial position of the probe 7
- H1: amount of movement of the probe 7 before the sample level is detected
- H2: height of the sample in the vessel 6A
- V1: volume of the sample
- S: bottom area of the vessel 6A

Therefore, V1 is determined as follows.

$$V1 = S \times H2 = S \times (H0 - H1) \quad (1)$$

An accuracy of the value V1 depends on such conditions as a dimensional accuracy of the sample vessel 6A, an accuracy of the positional relationship between the sample vessel 6A and the sample quantity determination probe 7, an accuracy of movement of the sample quantity determination probe 7, a sensitivity of the level detection unit 10, and the like. According to the present invention, however, when the error thereof are known, the object of the invention can be achieved. The error is now assumed as a value of Ve. Further, although the sample is sucked by the sample quantity determination probe 7, transferred to the measurement line 12 such as the route R2 and supplied to the reaction vessel 12A thereof, it is difficult to entirely suck the amount of the sample corresponding to V1 and thus it cannot be avoided that a slight amount of the sample remains. When this remaining amount is represented by Vd, an amount V2 to be used for measurement will be eventually expressed as follows.

$$V2 = V1 - Ve - Vd \quad (2)$$

Therefore, the amount V2 is sucked from the vessel 6A by the pump 8 through the sample quantity determination probe 7, transferred to the measurement line 12, and supplied to the reaction vessel 12A. Here, the amount V2 is naturally smaller than the amount V0 necessary for measurement. The insufficient amount V = (V0 - V2) is supplemented with pure water supplied from the dilution unit 13.

More specifically, the sample is diluted by a magnification ratio for dilution D shown by the following farmula.

$$D = (V2 + V)/V2 = V0/V2 \quad (3)$$

This magnification ratio for dilution D is stored in the measurement control unit 14.

The diluted sample is analyzed in the measurement line 12 in the same way as that of a usual sample for obtaining a measured value. Then, the measured value is multiplied by the magnification ratio for dilution D by means of the above measurement control unit 14 storing the same and converted to an actual concentration value, which is sent to the overall control unit 15 and reported to the display unit 16. It is to be noted that an additional display may be made to indicate that the insufficient amount of the sample has been diluted.

The operation of the present invention will be described hereunder.

As shown in Fig. 3, respective samples requested to be analyzed are contained in the sample vessels 1A in the sample setting unit 1 and sucked by the sample suction probe 2 2 in accordance with analysis items, and the suction monitor 3 detects whether or not each sample has been sucked in an amount necessary for analysis. The sample the sucked amount of which is determined insufficient as the result of the detection is transferred to the temporary sample storage unit 6 by the above sample suction probe 2 through the route R1 and supplied to the sample vessel 6A prepared there, as shown in Fig. 4.

The amount V1 of the insufficiently sucked sample is determined from the formula (1) in the temporary sample storage unit 6 by the way mentioned above. Further, the amount V2 of the sample capable of being used for measurement is determined on the basis of the formula (2), and furthermore, an insufficient amount is determined from the amount V0 necessary for measurement. In addition, a magnification ratio for dilution D fordetermining an amount to be added to the amount V2 is calculated on the basis of the formula (3) and stored inthe measurement control unit 14.

Subsequently, this sample is sucked by the sample quantity determination probe 7, transferred to the measurement line 12 through the route R2 and supplied to the reaction vessel 12A. Referring to Fig. 5, pure water of the amount corresponding to the above insufficient amount V is supplied to the sample in the reaction vessel 12A from the dilution unit 13 through the dilution probe 13A under the control of the measurement control unit 14 so that the magnification ratio for dilution D can be obtained. Thereafter, the sample is analyzed by a colorimetric method similarly to a usual sample to obtain a mesured value.

Next, the measured value is corrected by being multiplied with the magnification ratio for dilution D by the measurement control unit 14 and converted to an actual concentration value. The converted measured value is sent to the overall control unit 15 and then reported by being outputted to the monitor of the display unit 16 or being printed by a

printer as data corresponding to each measurement item.

Since the sample which is not determined to be sucked in an insufficient amount has no problem, it is transferred to the direct measurement line 12 through the route R3 in the state that it is sucked by the sample suction probe 2.

The above described processes will be briefly represented by flowcharts shown in Fig. 8.

Referring to Fig. 8, when it is required to carry out the sampling process, a sampling start instruction is first made and then, in step S1, the control unit instructs to the drive unit 5 so as to move the probe 2 for sucking the sample in the vessel 1A. In step S2, it is discriminated by the suction monitor 3 whether or not the predetermined amount of the sample can be sucked, and in case of YES, the sample vessel 1A is transferred directly to the reaction vessel 12A of the measurement line 12 and in case of No, that is, being discriminated that the sample amount is insufficient, the sample is delivered to the sample temporary storage unit 6.

In step S3, the sample quantity determination probe 7 is operated to determine the sample amount, that is, the top level of the sample in the vessel 6A is detected for ensuring the minimum amount of the sample sucked. This data is sent to the control unit 15 and the insufficient amount of the sample is calculated in step S4. In this step S4, the magnification ratio for dilution, in a case where the calculated insufficient amount of the sample is substituted by the pure water, is also calculated. The result of these calculations are stored in the measurement control unit 14. In the next step S5, in accordance with the above calculations, the sucked insufficient amount of the sample and the added dilution solution are transferred in the reaction vessel 12A.

The samples transferred to the measurement line 12 are subjected to the concentration calculation, step S6, to determine whether or not the sample in the reaction vessel 12A is the diluted sample, and in case of YES, in step S7, the concentration is converted into an actual concentration value by considering the magnification ratio for dilution. The result of this calculation is displayed to the monitor or printed by the printer as data in step S8. These processes are automatically repeated.

According to the present embodiment, even the sample the sucked amount of which is detected to be insufficient prior to analysis is transferred to the temporary sample storage unit 6 instead of being directly transferred to the measurement line 12. An insufficient amount of the sample is calculated and the magnification ratio for dilution for increasing the amount of the sample to an amount necessary for measuring the sample is determined in the sample temporary storage unit 6. Thereafter, the sample is transferred to the measurement line 12. The sample is measured in the same way as that of a usual sample of sufficient amount and the measured value is corrected on the basis of the magnification ratio for dilution. Therefore, even if a sample is insufficiently sucked, the sample is used as it is and subjected to analyzing process after having been diluted. Accordingly, the sample is not wasted. Further, since the sample need not be remeasured, a time consumed by the remeasurement is saved. It is also to be noted that since a method for determining the quantity of a sucked sample is not required to have a strict accuracy as compared with that required when a sample is sucked or discharged, this method can be realized within the range of usual technologies.

Further, since the process for determining a quantity of an insufficiently sucked sample by the sample quantity determination unit 7 in the temporary sample storage unit 6 is carried out concurrently with the usual process for sucking a sample from the sample vessel 1A by the sample suction probe 2, an analysis efficiency is not lowered at all.

Although the present invention is described with respect to an example in which the sample suction probe 2 is prepared independently of the sample quantity determination probe 7, a single probe acting as both the sample suction probe 2 and the sample quantity determination probe 7 may be used. Further, although a method of determining the quantity of a sample in the vessel 6A by the temporary sample storage unit 6 is described with reference to the example in which an amount of vertical movement of the sample quantity determination probe 7 is utilized, the present invention is not limited to this method, and a level height may be determined by using an optical method or a sucked amount may be set as V1 based on a change of a detection signal from the suction monitor 3 and the operation of the pump 4.

Claims

1. An automatic chemical analysis system in which a sample and a reagent supplied in a reaction vessel disposed in a measurement line are subjected to analysis treatment and analyzed result is then reported, comprising:

   means for sucking the sample from a sample vessel;

   means for detecting a fact as to whether a sucked amount of the sample is sufficient or insufficient for the analysis;

   means for calculating an insufficient amount of the sucked sample when it is detected by the detecting means that an insufficient amount of the sample necessary for the

analysis is sucked and for obtaining an information regarding an amount of a dilution solution for compensating for the insufficient amount of the sample;

means for carrying out an analysis treatment after dilution of the sample in accordance with the information of the amount of the dilution solution; and

means for compensating for a result of the analysis treatment in accordance with the information of the amount of the dilution solution.

2. An automatic chemical analysis system comprising:

a sample setting unit for accommodating a plurality of sample vessels each in which a sample is contained;

a suction unit for sucking the sample in the sample vessel and detcting an amount of the sucked sample;

a sample temporary storage unit for storing the sample vessel in which an insufficient amount of the sample is contained;

a dilution unit for diluting the sample contained in the sample vessel stored in the sample temporary storage unit;

a reagent setting unit for supplying a reagent into the sample vessel;

a measurement unit including a sample reaction vessel into which the reagent is additionally supplied from the reagent setting unit;

means for controlling operations of the suction unit, the sample temporary storage unit and the dilution unit, said control means including an element for instructing that a sample vessel containing the sufficient amount of the sample is to be directly transferred to the measurement unit and a sample vessel containing the insufficient amount of the sample is to be transferred to the sample temporary storage unit, an element for calculating an insufficient amount of the sucked sample in the sample vessel transferred to the sample temporary storage unit and for obtaining an information regarding an amount of a dilution solution for compensating for the insufficient amount of the sample, an element for carrying out an analysis treatment after dilution of the sample in accordance with the information of the amount of the dilution solution and an element for compensating for a result of the analysis treatment in accordance with the information of the amount of the dilution solution; and

means for displaying a result of the analysis of the sample.

3. An automatic chemical analysis system according to cliam 2, wherein the suction unit includes a sample suction probe for sucking the sample from the sample vessel disposed in the sample setting unit and a suction monitor for detecting the fact as to whether or not the sufficient amount of the sample is sucked.

4. An automatic chemical analysis system according to claim 2, wherein the sample temporary storage unit includes a sample quantity determination probe for determining an amount of the sample in the sample vessel transferred to the sample temporary storage unit, said sample quantity determination probe being provided with a level sensor for detecting a surface level of the sample contained in the sample vessel.

5. An automatic chemical analysis system according to claim 2, wherein the dilution solution is pure water and the sample of the insufficient amount is diluted by the pure water with a calculated magnification ratio of dilution.

6. An automatic chemical analysis system according to claim 5, wherein the result of the analysis treatment is converted into an actual concentration value by considering the magnification ratio of dilution.

7. An automatic chemical analysis method for sucking a sample in a sample vessel and analyzing the sample in a measurement line, comprising the steps of:

sucking a sample from the sample vessel;

discriminating whether the sucked samle has a sufficient or insufficient amount;

transferring a sample discriminated to have a sufficient amount directly to a measurement line and separately transferring a sample discriminated to have an insufficient amount;

calculating an insufficient amount of the separately transferred sample;

calculating a magnification ratio for dilution for the sample of the insufficient amount;

supplying a dilution solution by an amount in accordance with the caluculated magnification ratio for dilution;

transferring the thus diluted sample to the measurement line;

calculating concentration of the samples transferred to the measurement line;

calculating an actual concentration with respect to the diluted sample in accordance with the magnification ratio for dilution; and

carrying out a chemical analysis of the sample.

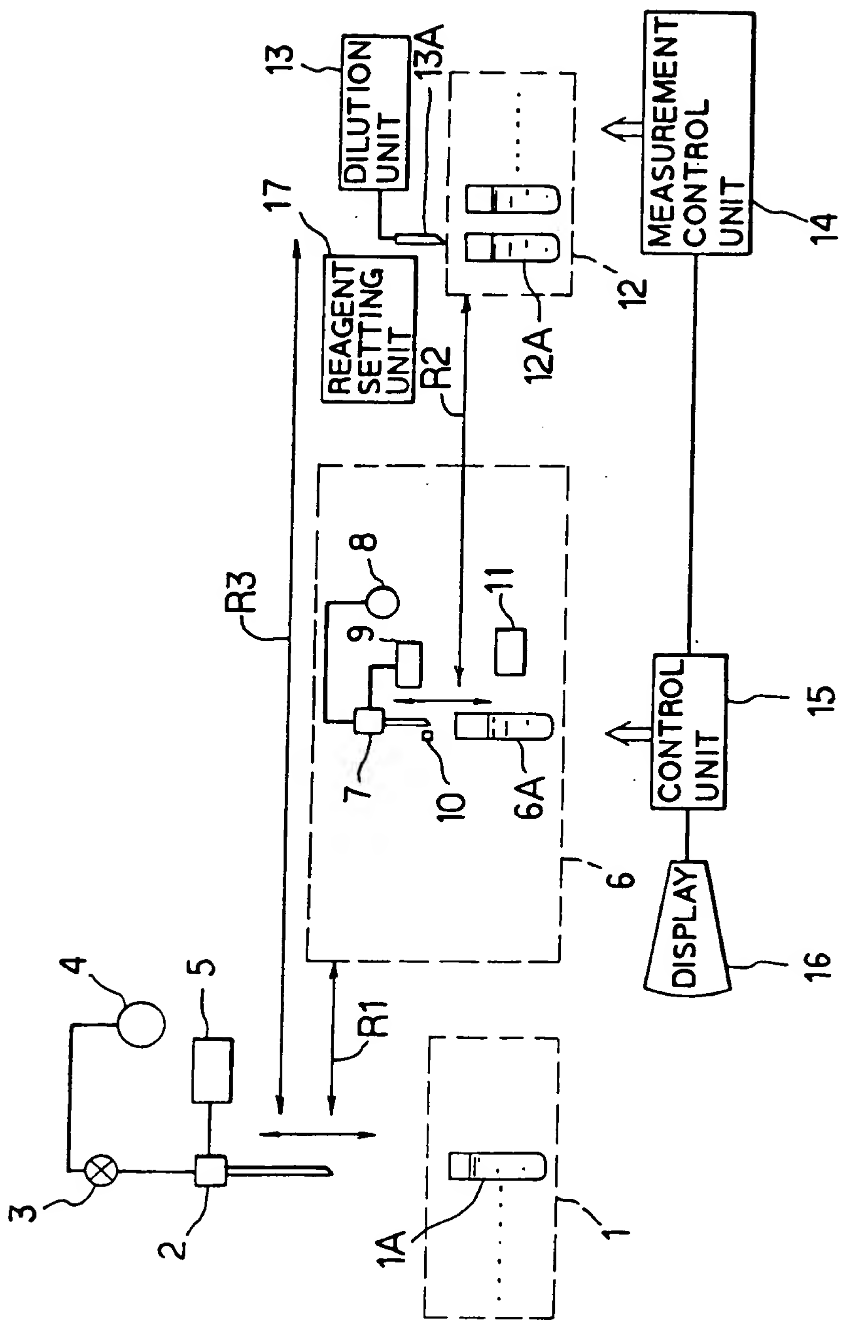
DILUTION UNIT
13
13A
17
REAGENT SETTING UNIT
R2
12
12A
MEASUREMENT CONTROL UNIT
14
R3
8
9
11
7
10
6A
6
CONTROL UNIT
15
DISPLAY
16
4
5
3
2
R1
1A
1

FIG. 1

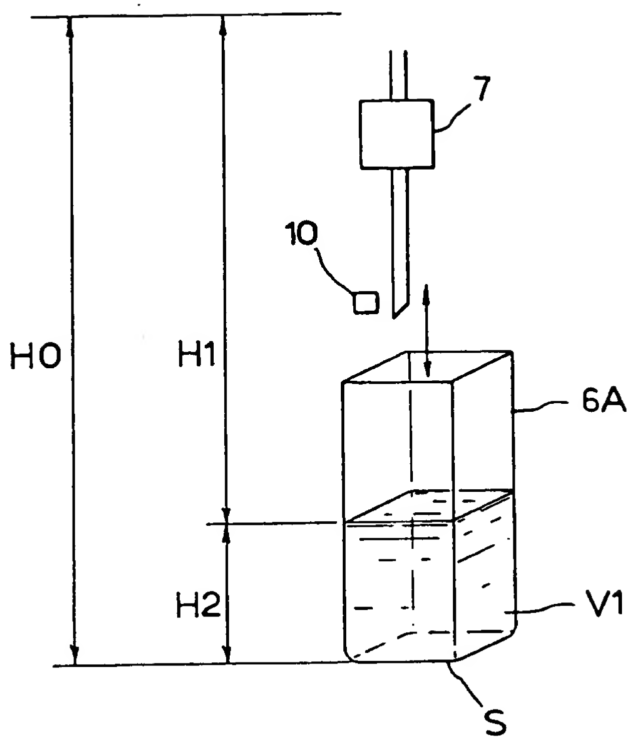
7
10
H0
H1
6A
H2
V1
S

FIG. 2

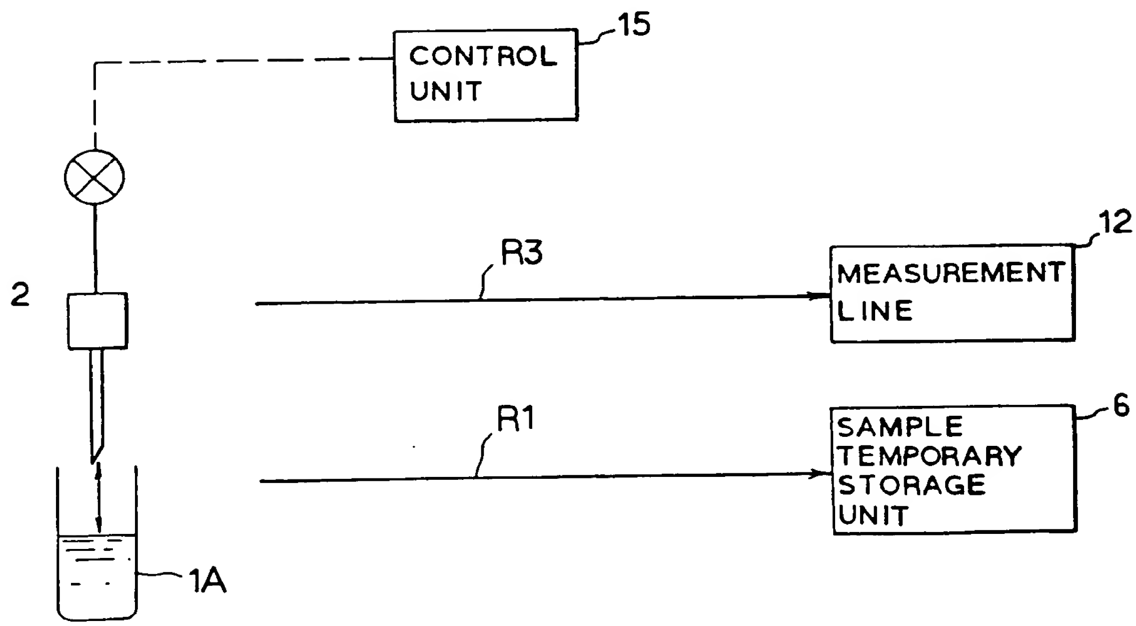
CONTROL UNIT
15
12
R3
2
MEASUREMENT LINE
R1
6
SAMPLE TEMPORARY STORAGE UNIT
1A

FIG. 3

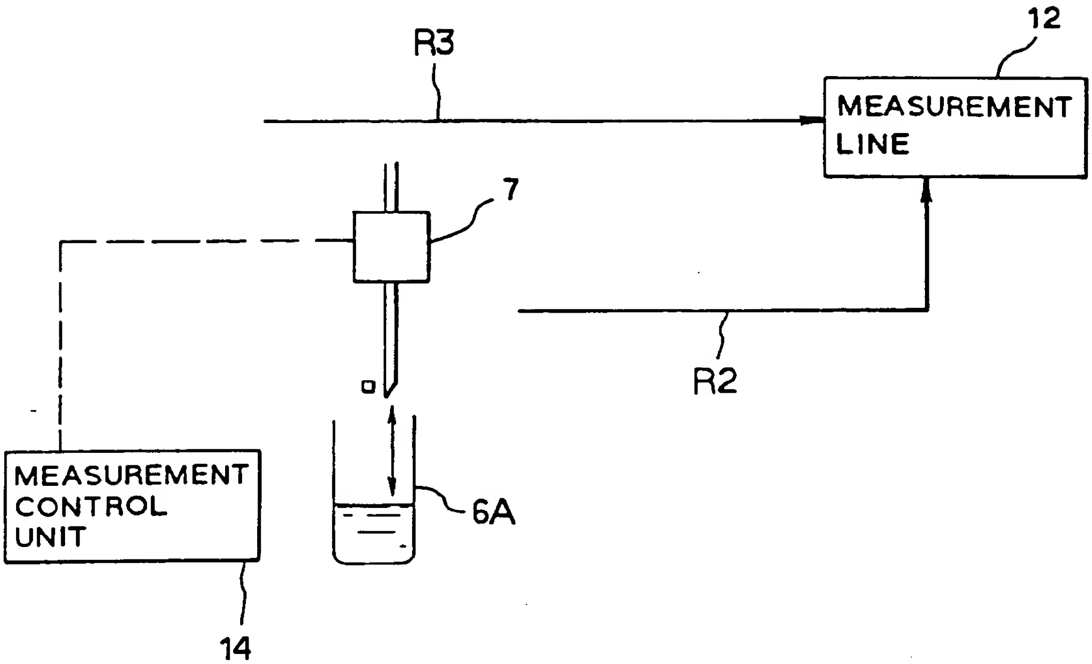
R3
12
MEASUREMENT LINE
7
R2
MEASUREMENT CONTROL UNIT
6A
14

FIG. 4

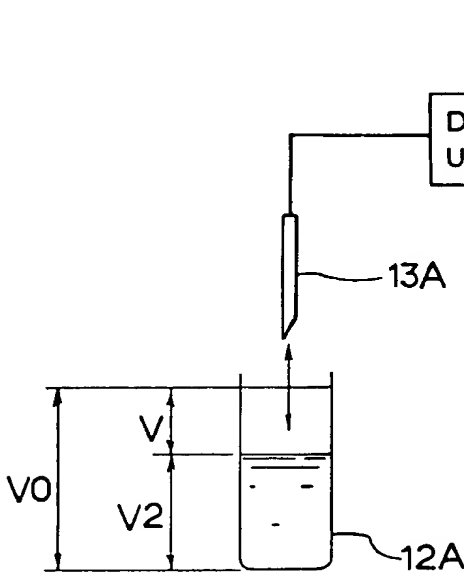
13
DILUTION UNIT
13A
V
V0
V2
12A

FIG. 5

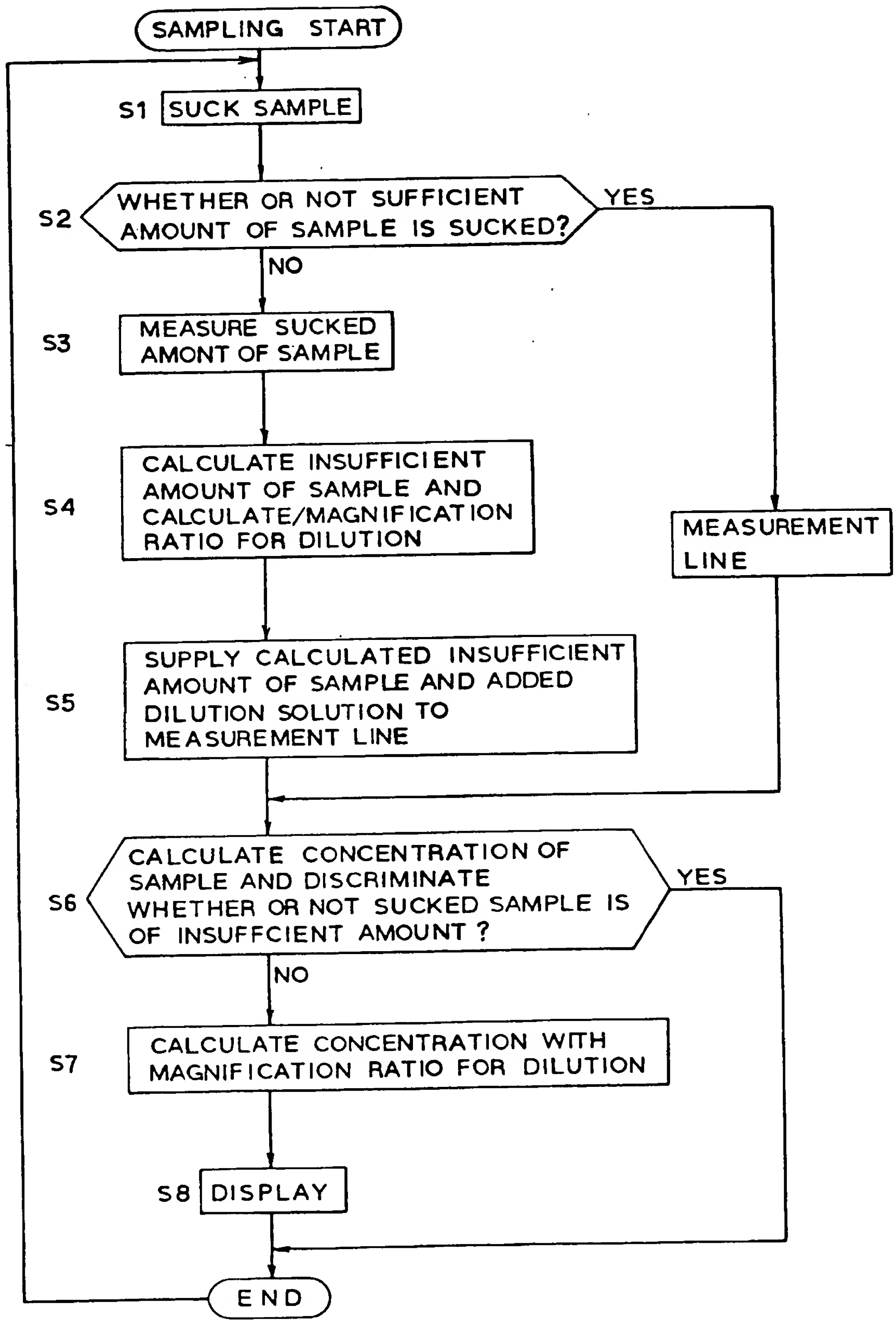
SAMPLING START
S1
SUCK SAMPLE
S2
WHETHER OR NOT SUFFICIENT AMOUNT OF SAMPLE IS SUCKED?
YES
NO
S3
MEASURE SUCKED AMONT OF SAMPLE
S4
CALCULATE INSUFFICIENT AMOUNT OF SAMPLE AND CALCULATE/MAGNIFICATION RATIO FOR DILUTION
MEASUREMENT LINE
S5
SUPPLY CALCULATED INSUFFICIENT AMOUNT OF SAMPLE AND ADDED DILUTION SOLUTION TO MEASUREMENT LINE
S6
CALCULATE CONCENTRATION OF SAMPLE AND DISCRIMINATE WHETHER OR NOT SUCKED SAMPLE IS OF INSUFFCIENT AMOUNT ?
YES
NO
S7
CALCULATE CONCENTRATION WITH MAGNIFICATION RATIO FOR DILUTION
S8
DISPLAY
END

FIG. 6

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: 0 506 022 A3

(12) # EUROPEAN PATENT APPLICATION

(21) Application number: 92105149.6

(51) Int. Cl.5: G01N 35/06, G01N 1/28

(22) Date of filing: 25.03.92

(30) Priority: 26.03.91 JP 61669/91

(43) Date of publication of application: 30.09.92 Bulletin 92/40

(84) Designated Contracting States: DE

(88) Date of deferred publication of the search report: 20.01.93 Bulletin 93/03

(71) Applicant: Kabushiki Kaisha Toshiba
72, Horikawa-cho Saiwai-ku
Kawasaki-shi(JP)

(72) Inventor: Shinohara, Hiroo
70-32, Higashimishima 4-Chome,
Nishinasuno-Machi
Nasu-Gun, Tochigi-ken(JP)

(74) Representative: Blumbach Weser Bergen
Kramer Zwirner Hoffmann Patentanwälte
Radeckestrasse 43
W-8000 München 60(DE)

(54) Automatic chemical analysis system and automatic chemical analysis method.

(57) An automatic chemical analysis sytem comprises a sample setting unit (1) for accommodating a plurality of sample vessels (1A) each in which a sample is contained, a suction unit (2) for sucking the sample in the sample vessel and detcting an amount of the sucked sample, a sample temporary storage unit (6) for storing the sample vessel in which an insufficient amount of the sample is contained, a dilution unit (13) for diluting the sample contained in the sample vessel stored in the sample temporary storage unit, a reagent setting unit (17) for supplying a reagent into the sample vessel, a measurement unit (12) including a sample reaction vessel into which the reagent is supplied from the reagent setting unit (17), and a control unit (15) for controlling operations of these units. The control unit (15) performs operations for instructing that a sample vessel containing the sufficient amount of the sample is to be directly transferred to the measurement unit (12) and a sample vessel containing the insufficient amount of the sample is to be transferred to the sample temporary storage unit (6), for calculating an insufficient amount of the sucked sample in the sample vessel transferred to the sample temporary storage unit (6) and for obtaining an information regarding an amount of a dilution solution for compensating for the insufficient amount of the sample, for carrying out an analysis treatment after dilution of the sample in accordance with the information of the amount of the dilution solution, and for compensating for a result of the analysis treatment in accordance with the information of the amount of the dilution solution.

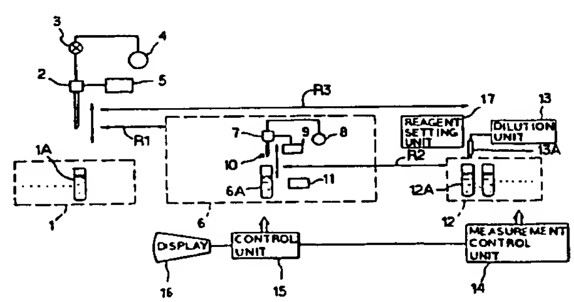

FIG. 1

EP 0 506 022 A3

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 92 10 5149

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
P,X	PATENT ABSTRACTS OF JAPAN vol. 015, no. 363 (P-1251)12 September 1991 & JP-A-31 40 844 (SHIMADZU CORP) 14 June 1991 * abstract *	1	G01N35/06 G01N1/28
P,A	---	2,4,6,7	
A	US-A-4 130 394 (NEGERSMITH) * abstract; figure 1 * ---	1-3,7	
A	EP-A-0 255 026 (TAKEDA CHEMICAL INDUSTRIES) * abstract * * page 3, line 1 - line 8; claims 1,2 * ---	4,5	
A	US-A-4 591 568 (BANNO ET AL) * abstract * -----	1-3,7	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

G01N

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	11 NOVEMBER 1992	MILLS J.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document